REMARKS

Claims 1, 5, and 7-10 have been amended to more particularly point out and distinctly claim certain embodiments of Applicants' invention and to correct typographical errors. Support for the amendments to the claims can be found throughout the specification and claims as originally filed, e.g., in Examples 4, 19, 30 and 31. Claims 3, 6 and 11-12 have now been cancelled without prejudice or disclaimer. Upon entry of this amendment, claims 1, 4-5, and 7-10 will be pending in the application. No new matter has been added.

The amendment and/or cancellation of claims is without prejudice or disclaimer of the subject matter thereof and was done solely to expedite prosecution of the present application. Applicants reserve the right to pursue the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject mattered.

Rejection of Claims under 35 USC §103(a)

Claims 1-3 and 5-12 were rejected under 35 USC §103(a)as being allegedly unpatentable over Sekine (WO 96/04902 and US Patent equivalent) in view of Inagi et al. The rejection is traversed.

As the reference is understood, Sekine teaches that it is possible to obtain a composition for external application comprising a water-soluble salt of diclofenac and to use said composition to make some preparations such as cataplasm. Benzalconium chloride is mentioned as one of the examples of antiseptics as additives. However, Applicants contend that there is no example in Sekine of a composition comprising both sodium dichlorofenac and ammonium chloride, much less a composition in which the ammonium chloride is blended at the range of from 0.5 to 10 fold mole based on the sodium dichlorofenac, as recited by claims 1 and 10 (all remaining claims depend, directly or indirectly, from claim 1).

According to the Examiner, Inagi describes "an adhesive plaster comprising an acrylic polymer . . . [a]ntiseptics such as benzalkonium chloride, are disclosed at 0.01-5%." However, the Examiner has not cited the Inagi reference as containing any teaching or suggestion of a composition comprising both sodium dichlorofenac and ammonium chloride, much less a composition in which the ammonium chloride is blended at the range of from 0.5 to 10 fold mole based on the sodium dichlorofenac, as recited by the pending claims.

As neither reference contains any teaching or suggestion of the presently-claimed subject matter, Applicants respectfully contend that neither Sekine nor Inagi, whether taken alone or in combination, can render the claimed invention obvious.

Furthermore, as illustrated by the data presented in, e.g., Tables 1 and 2 of the instant application, the presently-claimed preparations can exhibit large increases in percutaneous absorption of sodium dichlorofenac in comparison with a preparation which does not include ammonium chloride.

Applicants further submit that the present claims patentably distinguish the document CN1171736, cited in the Information Disclosure Statement (IDS) filed on January 20, 2006 (see below) and its equivalent, U.S. Patent No. 5,866,157 (cited in the IDS filed on even date herewith).

Finally, Applicants submit that the present claims patentably distinguish the document JP04-217925 (submitted in an IDS on even date herewith, with a partial English translation). Applicants therefore contend that the present claims are patentable over the references of record, whether the references are taken alone or in any combination.

Reconsideration and withdrawal of the rejection is proper and such action is requested.

Objections to the Claims

The Examiner objected to claim 6 as allegedly vague, stating that "it is unclear as to whether a matrix is definitely claimed." Applicants respectfully contend that this language would be understood by one of ordinary skill in the art, and refers to a device for transdermal drug delivery wherein the drug is dissolved or dispersed in a polymer phase and the drug release from the drug/polymer matrix controls the overall rate of its release from the device. As evidence of the use of the terminology in the relevant art, submitted herewith is a copy of a portion of A. Kydonieus (Ed.), "Treatise on Controlled Drug Delivery: Fundamentals, Optimization, Application", Marcel Dekker, New York (1992), p. 399 (see, e.g., lines 8-10 and 28-29 and Figure 32). Accordingly, Applicants submit that the claim language is not vague or indefinite and does comply with the requirements of, *inter alia*, 35 U.S.C. §112.

Claim 9 was objected for reciting the word "styylene". The claim has been amended to replace "sstylene" with "stylene."

Reconsideration and withdrawal of the objections is proper and such action is requested.

Information Disclosure Statements

Applicants note that an IDS was filed on January 20, 2006, and an additional IDS is being filed herewith. Applicants note that U.S. Patent No. 5,866,157 (cited in the IDS of even date) is an equivalent of CN1171736, cited in the IDS filed on January 20, 2006. Applicants respectfully request that the Examiner consider the IDSs and return an initialed copy of the forms PTO/SB08/08a/b with the next Office Action or Notice of Allowance.

Conclusion

For at least the foregoing reasons, Applicants request reconsideration of the application. Early and favorable action is requested.

The undersigned requests any extension of time necessary for response. Although it is not believed that any additional fees are needed to consider this submission, the Examiner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

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TRANSDERMAL DEVICES

Devices for transdermal drug delivery are generally fabricated as multilayered polymeric laminate structures in which a drug reservoir or a drug/polymer matrix is sandwiched between two polymeric layers. The outer backing layer, comprising an impermeable polymer or a foil, is designed to prevent loss of drug through the backing surface. The other polymeric layer may function as an adhesive or a rate-controlling membrane (Fig. 32). Based on the mechanism by which the drug is released, the device can be classified into one of the following two categories.

Monolithic (or matrix) system: The drug is dissolved or dispersed in the polymer phase. The drug release from the drug/polymer matrix controls the overall rate of its release from the device (Fig. 32a).

Reservoir (or membrane) system: Diffusional resistance across a polymeric membrane controls the overall drug release rate (Fig. 32b).

The selection of either a monolithic or a reservoir system for transdermal drug delivery depends on which is a major contributing factor controlling the rate of drug transport and its delivery to the systemic circulation. The total resistance to drug transport from the device across the skin can be considered to be the sum of the diffusional resistances through the device (R_1) and that through the stratum corneum (R_2). It may be assumed that the epidermal resistance is negligible compared with that of the stratum corneum. In general, analogous to the current flow in an electrical circuit having resistances connected in series, the overall rate of drug transport will be inversely proportional to the sum of the two resistances ($R_1 + R_2$). If $R_2 \gg R_1$, the overall rate of drug transport will be governed by the rate of drug permeation through the stratum corneum. And if $R_1 \gg R_2$, the device will control the overall rate.

When the desired rate of drug transport is considerably less than that through the stratum corneum, a device control of drug delivery is required to attain therapeutic steady-state concentrations of drug in the blood plasma and prevent overdosing. In such cases, a device having a rate-controlling membrane is needed. On the other hand, if drug permeation through the stratum corneum is the rate-controlling step, a monolithic or matrix type of delivery system may suffice. The therapeutic index of the drug and the variations in its skin permeability for any given population are also important criteria in selecting the type of transdermal device. If the therapeutic index is narrow in relation to the range of systemic drug concentration attained due to the variability in its skin permeation characteristics, a monolithic system would not be suitable.

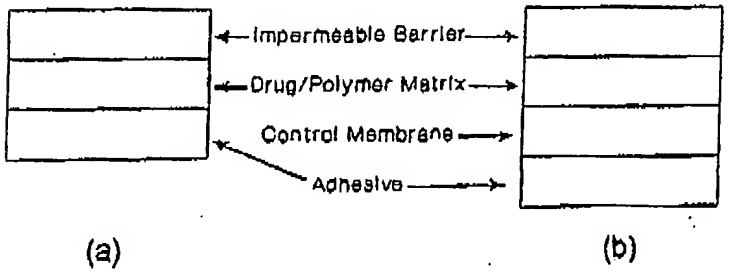

Figure 32 Schematic diagrams of laminated transdermal devices: (a) matrix system; (b) membrane system.